

The Indiana Division of Mental Health and Addiction (DMHA) in collaboration with its integration stakeholder cross agency partners submitted a Technical Transfer Initiative (TTI) grant proposal and was awarded funding from the Substance Abuse and Mental Health Services Administration (SAMHSA) through the National Association of State Mental Health Program Directors (NASMHPD). That grant is supporting today's training activities.

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Psychopharmacology for Common Illnesses and Working with Psychiatric Providers

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Module 4

Psychopharmacology for Common Illnesses and Working with Psychiatric Providers

- Learning Objectives:
- Understand the most commonly used psychotropic medications and their potential side effects
- Discuss the problems associated with psychotropic prescribing and the role of the PCP-Psychiatric provider liaison in minimizing risk
- Appreciate the need to work with psychiatric provider colleagues on ownership of prescribing and rules of engagement

Pre Course Questions

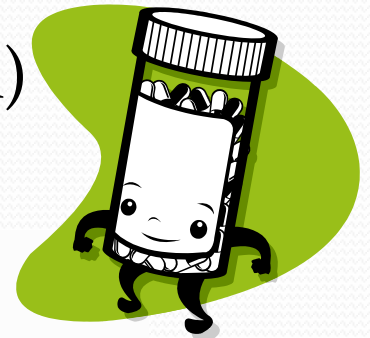
1. Which SGAs lead to the most weight gain?
 1. Olanzapine (Zyprexa) and Quetiapine (Seroquel)
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 4. Haloperidol (Haldol) and Fluphenazine (Prolixin)
2. Which tests are recommended by the ADA/APA guidelines for SGAs?
 1. Lipid Panel
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 3. BMI
 4. All the above
3. What percentage of patients with Schizophrenia smoke?
 1. ~30 - 40%
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4. What roles do the psychiatric providers play in the medical treatment of their patients?
 1. Minimize risk by selection of medications
 2. Screen for medical complications of medications
 3. Counsel on lifestyle modification
 4. All of the above

Overview

- Medication Classes
- Anxiety
- Sleep
- Smoking
- Substance Use
- Pain
- Psychiatric Providers

Classes of Psychotropic Medications

- Antipsychotics – 1st and 2nd Generation (SGA)
- Antidepressants – TCA, SSRI, SNRI, SDRI
- Mood Stabilizers
- Anxiolytics



First Generation (FGA) Antipsychotics

Yes, we still use them....Potent D2 receptor

- High Potency – decanoate helpful for homeless, few social supports, frequent relapse
- Fluphenazine (Prolixin) also has decanoate formulation
- Haloperidol (Haldol) also decanoate
- Low Potency – dopamine + histamine, acetylcholine, muscarinic
 - Thioridazine (Mellaril)
 - Loxapine (Loxatane)
 - Chlorpromazine (Thorazine)
 - Thiothixene (Navine)
 - Perphenazine (Trilafon)



FGA Side Effects – think Parkinson's

- Dyskinesias – movement disorder (nigrostriatal dopamine pathway)
tongue, lips, eye, limbs, fingers
Tardive Dyskinesia – can be permanent
- Dystonias – muscle tension
neck (torticollis), arms, legs – any body part
painful – benztropine, diphenhydramine to treat – IM available
- Akathisia – extreme restlessness
hard to sit still, pacing, shakiness – can be exhausting,
reduce dose
- Hyperprolactinemia – D2 blockade (tubuloinfundibular dopamine pathway)
amenorrhea, galactorrhea – lower the dose, switch, work with GYN

DECADE OF THE BRAIN

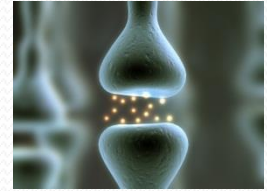
1990 – 1999

July 17, 1990

Now, Therefore, I, George Bush, President of the United States of America, do hereby proclaim the decade beginning January 1, 1990, as the Decade of the Brain.

Many new medications introduced with novel mechanisms of action during this decade

Decade of the Brain from the Trenches



Antidepressants

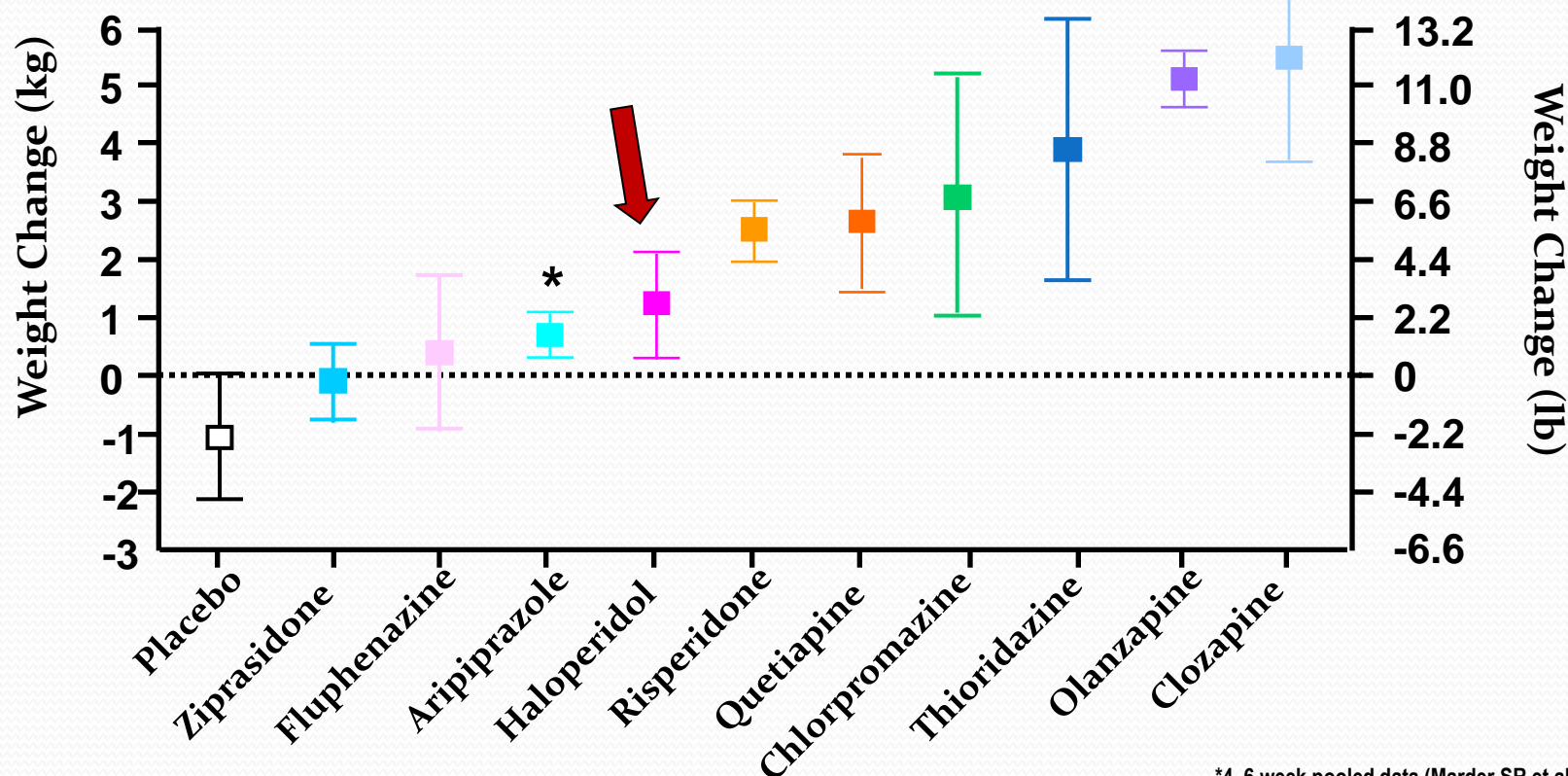
- 1987 – Prozac (fluoxetine)
- 1989 – Celexa (citalopram)
- 1989 – Wellbutrin (bupropion)
- 1992 – Zoloft (sertraline)
- 1992 – Paxil (paroxetine)
- 1993 – Luvox (fluvoxamine)
- 1993 – Effexor (venlafaxine)

Second Generation Antipsychotics (SGA/”Atypical”)

- 1991 – Clozaril (clozapine)
- 1994 – Risperdal (risperidone)
- 1994 – Zyprexa (olanzapine)
- 1995 – Seroquel (quetiapine)
- 2001 – GeoDon (zispriazidone)
- 2002 – Abilify (aripiprizole)
- x

We started to notice some problems....

Estimated Weight Change at 10 Weeks on “Standard” Dose



*4–6 week pooled data (Marder SR et al. *Schizophr Res.* 2003;1;61:123-36; 16-week data adapted from Allison DB, Mentore JL, Heo M, et al. *Am J Psychiatry.* 1999;156:1686-1696; Jones AM et al. *ACNP*; 1999.

These risk factors already existed

Modifiable Risk Factors	Estimated Prevalence and Relative Risk (RR)	
	Schizophrenia	Bipolar Disorder
Obesity	45–55%, 1.5-2X RR ¹	26% ⁵
Smoking	50–80%, 2-3X RR ²	55% ⁶
Diabetes	10–14%, 2X RR ³	10% ⁷
Hypertension	≥18% ⁴	15% ⁵
Dyslipidemia	Up to 5X RR ⁸	42%

1. Davidson S, et al. *Aust N Z J Psychiatry*. 2001;35:196-202. 2. Allison DB, et al. *J Clin Psychiatry*. 1999; 60:215-220.

3. Dixon L, et al. *J Nerv Ment Dis*. 1999;187:496-502. 4. Herran A, et al. *Schizophr Res*. 2000;41:373-381.

5. MeElroy SL, et al. *J Clin Psychiatry*. 2002;63:207-213. 6. Uçok A, et al. *Psychiatry Clin Neurosci*. 2004;58:434-437.

7. Cassidy F, et al. *Am J Psychiatry*. 1999;156:1417-1420. 8. Allebeck. *Schizophr Bull*. 1999;15(1)81-89. 9. VanCampfort, AJP, 2013

SGA Side Effects - “an epidemic within an epidemic”

Medication	Diabetes	EPS	Prolactin	QT Interval	Weight
Aripiprazole	+/-	+	+/-	+/-	+
Asenapine	+	+++	++	+	++
Clozapine	+++++	+/-	+/-	+	+++++
Illoperidone	++	+	+/-	++	++
Lurasidone	+/-	++	+	+/-	+/-
Olanzapine	+++++	+	+	+	+++++
Paliperidone	++	+++	+++	+	+++
Quetiapine	++	+/-	+/-	+	+++
Risperidone	++	+++	+++	+	+++
Ziprasidone	+/-	+	+	++	+/-

ADA/APA Screening Guidelines for Second Generation Antipsychotics

	Baseline	4 wks	8 wks	12 wks	Annually
Review Personal / Family history of illness	X				X
Weight [BMI]	X	X	X	X	X
Waist Circumference	X			X	X
Blood Pressure	X			X	X
Fasting Plasma Glucose	X			X	X
Fasting Lipid Profile	X			X	X

American Association of Clinical Endocrinologists, North American Association for the Study of Obesity: Consensus development conference on antipsychotic drugs and obesity and diabetes. Diabetes Care 2004; 27:596-601

Newer SGAs – promise of fewer cardiovascular complications?

Drug	Dose Range	Side Effects
Lurasidone (Latuda)	40 – 120 mg	Drowsiness, akathisia, no weight gain/metabolic
Asenapine (Saphris)	20 – 80 mg	Drowsiness, no weight gain/metabolic
Iloperidone (Fanapt)	6 – 12 mg	Dizziness, dry mouth, fatigue

Long-acting Injectable SGAs

- Risperdal Consta every 2 weeks
- Invega Sustenna monthly
- Abilfy Maintena monthly
- Zyprexa Relprevv monthly - *PDSS* risk: Post-Injection Delirium Sedation Syndrome – 3 hour watch

Clozapine (Clozaril)

- SGA used in treatment resistant patients
- Last resort due to life threatening agranulocytosis
- Weekly CBC x 6 months, then q 2 weeks
- Only registered pharmacies may dispense and must have CBC at pharmacy or will not get drug
- Absolute Neutrophil Count (ANC) >2
- “Clozaril clinics” in some sites due to volume and monitoring
- Therapeutic level ~ 200 – 400 ng/ml
- Same APA/ADA screening guidelines apply due to CV risk

CATIE Trial

- The NIMH-funded Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Study was a nationwide public health-focused clinical trial that compared the effectiveness of older (first available in the 1950s) and newer (available since the 1990s) antipsychotic medications used to treat schizophrenia. \$42.6 million study was conducted over a five-year period at 57 clinical sites across the country.

- **Perphenazine:**
(FGA)



- Olanzapine, risperidone, ziprasidone, quetiapine
(SGA)

- *Perphenazine (the older medication) equally as effective as the other three newer medications (risperidone, quetiapine, and ziprasidone) and was as well tolerated as the newer drugs. The three newer medications performed similarly to one another. Slight clinical advantage with olanzapine. No substantial advantage of newer medications.*

So why did we continue to use SGAs with CATIE trial results?

- **Efficacy
- **Less sedation/more sedation
- **Patient preference
- Low incidence of extra pyramidal symptoms
- Low incidence of tardive dyskinesia
- Cannot tolerate alternatives


Psych Services, 2013, Hermes, et al.
Prescription of Second Generation
Antipsychotics: Responding to Treatment
Risk in Real World Practice

Why Not Just Switch?

- If switch could get weight loss, lower FBS, favorable lipid profile, right?
- **Problems that might occur:**
 - rebound worsening of psychotic symptoms,
 - side effects, such as the addition of side effects of the old and new drugs, or side effects specific to the new drug, or
 - differences in efficacy between the drugs and concerns about unequal efficacy
 - problems might be specific to the discontinuation of the drug or to the drug to which the patient is switched.
- **The strategy (sometimes called 'overlap and taper')**
 - slow tapering of the initial antipsychotic after the new drug had been titrated to the *full dose*
 - ensures that the patient is covered with an adequate plasma level of the added drug before the former drug is discontinued
 - produces fewer problems during the switch than abrupt discontinuation or gradual discontinuation before starting a new drug.

[Cochrane Database Syst Rev.](#) 2010 Dec 8;(12):CD006629.
BMC Medicine 2008, 6:18

Mood Stabilizers - TMAP

Medication	Dose	Therapeutic Level	Side Effects	Labs	Cost
Lithium	Varies – start at 300 mg hs	Active 0.8 – 1.2 Maint 0.6 – 0.8 Toxic >1.5  *narrow window	Polyuria, GI, renal, thyroid, wt, loop diuretics, NSAIDS	12 hr trough TSH Cr	\$4
Valproic Acid	Varies – start at 500 mg	Active 80 – 100 Maint 60 – 80	Hepatic, wt, Platelets, GI Sedation	12 hr trough LFTs CBC	\$4
Carbamazapine	Varies – start at 200 mg	none	Sedation, wt WBC, GI, Hepatic	12 hr trough WBC LFTs	\$4
Lamotrigine (depression)	50 – 400	none	Rash, slow titration	none	\$\$
SGAs	varies	none	See previous	See previous	\$\$\$

Texas Medication Algorithm Project

Antidepressant Categories

SSRIs

- fluoxetine, paroxetine, citalopram – all \$4
- sertraline, escitalopram

SDRIs

- bupropion

SNRIs

- venlafaxine
- duloxetine

TCAs

- nortriptyline, imipramine, desipramine
- amitriptyline

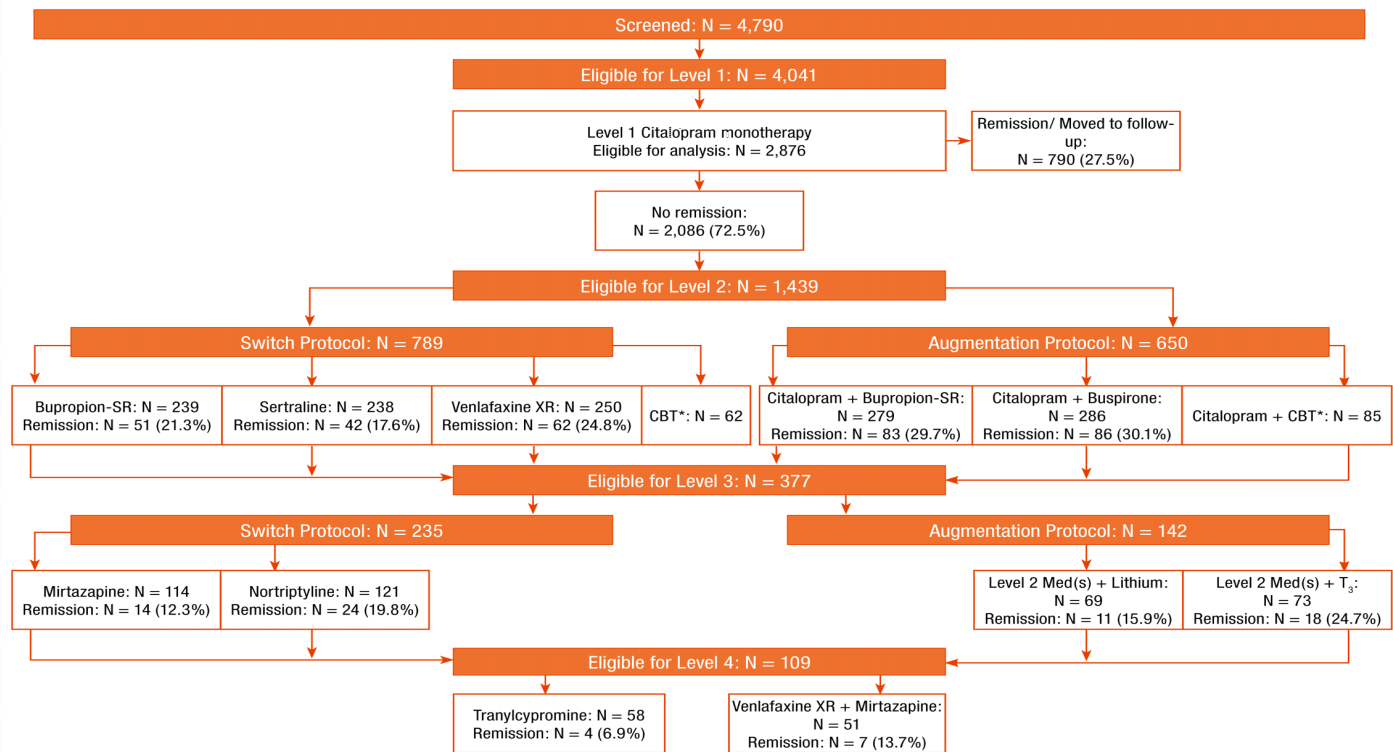
Other

- remeron, trazodone, vilazadone

NIMH STAR*D, \$35 MILLION, 6 YEAR “Real World” Study of Antidepressant Prescribing

On the Road to Remission

NIMH's STAR*D study involved a complex four-level protocol in which all patients started with SSRI monotherapy. For those patients who did not achieve remission (HamD-17 ≤ 7) or experienced intolerable side effects, multiple treatment options were available within levels 2 through 4. Upon achieving remission, patients were moved to a naturalistic follow-up phase of the study lasting as long as 12 months.



* No data published to date

Data compiled from: *Am J Psychiatry* (Jan 2006), *N Eng J Med* (March 23, 2006), *Am J Psychiatry* (July 2006) & *Am J Psychiatry* (Sept. 2006)

Side Effects Antidepressants

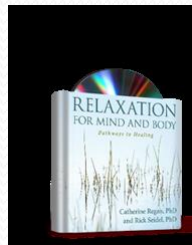
- SSRIs
insomnia
sexual side effects
weight gain
activation
nausea/diarrhea
- Norepinephrine
blood pressure
sedation
weight gain
cardiac in overdose

- Dopaminergic
activation
insomnia
no sexual SE
no weight gain
seizure risk
- SNRI
combo
nausea
weight gain
blood pressure changes

Approaches to Anxiety

Relaxation Exercises
Cognitive Behavioral Therapy

- SSRIs, SNRIs (first line med)
- Fluoxetine, paroxetine, sertraline, citalopram
- Duloxetine, venlafaxine



- Others
- Benzodiazepines –
 - Alprazolam (3hr half life)
 - lorazepam (8 hr half life),
 - clonazepam (18 hr half life)
- Gabapentin – 300 – 3000 mg (wt gain, loopiness)
- Buspirone
- SGAs
- B blockers
- *NOT Bupropion!*

Rational Approach to Benzodiazepines

- Efficacy, rapid onset make them desirable
- Acute stress, fluctuating anxiety, severe panic
- Limit use to acute episode if possible (4 weeks max) – can get difficult to stop these though
- Use in conjunction with other strategies – SSRI, therapy
- Base choice on half-life:
 - short anxiety attacks, events – alprazolam (3 hours)
 - sleep, intermediate coverage – lorazepam (6-8 hour)
 - longer term coverage – clonazepam (18 hours)

Drugs. 1994 Jul;48(1):25-40

Sleep

Sleep hygiene first! Naps common due to medication side effects and interfere with nl sleep patterns

Trazodone 25 – 200 mg

Gabapentin 300 – 900 mg

Mirtazapine 15 mg

SGAs – especially quetiapine

Benzodiazepines

Zolpidem - generic



Chronic Pain

- SNRIs – Venlafaxine, duloxetine – some additional benefit with chronic pain due to norepinephrine activity
- Gabapentin – up to 3,000 mg – watch dizziness, weight gain, renal clearance
- Narcotics are CNS depressants so interfere with antidepressant action. Many chronic pain patients are depressed.



Polypharmacy

- 40% of patients with schizophrenia took 2 antipsychotics
 - Add on quetiapine for sleep common
- Common: 1 or 2 antipsychotics, med for side effects, antidepressant, anxiolytic
- **Reconciliation with other meds important and difficult to accomplish. Use your Care/Case managers, EMR
- Work as a team with your psychiatric providers to avoid duplication
- Find non-pharmacologic interventions when possible

Ganguly R. J Clin Psych 2004

Day in the life of a Psychiatric Provider

- 49 yo female, Anxiety, citalopram 40 mg (the easy one – not SMI)
- 53 year old female, Bipolar I, lamotrigine 400 mg, Abilify 15 mg, chlorpromazine 300 mg, fluvoxamine 100 mg
- 33 year old male, Schizoaffective DO, Invega Sustenna, sertraline 100 mg, trazodone 100 mg, trileptal 300 bid
- 28 year old male, Schizoaffective DO, Invega Sustenna 234 mg, Invega 6 mg, Trazodone 100 mg, Depakote 1000 mg
- 41 year old female, Schizophrenia, olanzapine 10 mg, topomax 100 mg bid, trazodone 100 mg
- 53 year old male, Schizophrenia, Invega Sustenna, Bupropion SR 300 mg, trazodone 150 mg, citalopram 40 mg

Non Pharmacologic Approaches: Evidence Based Therapies

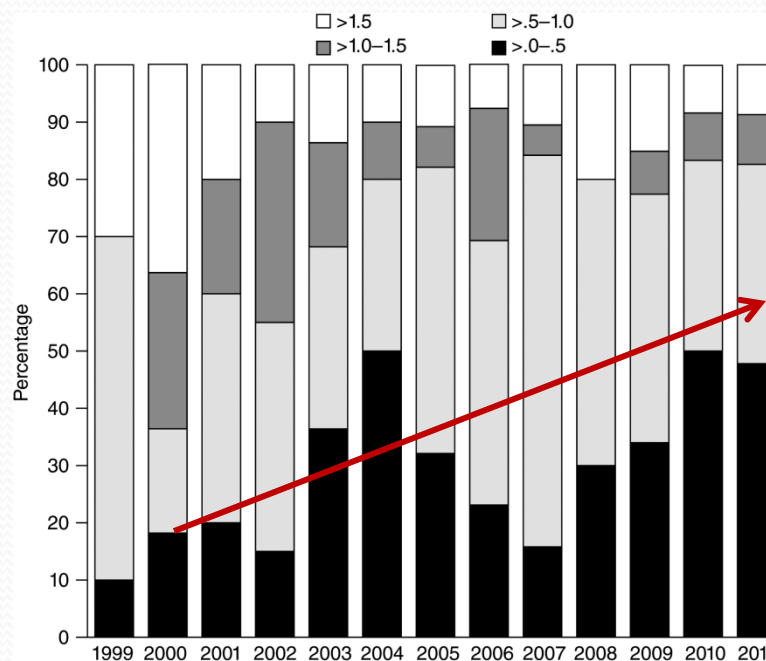
- Cognitive Behavioral Therapy (CBT) for residual psychotic symptoms and anxiety disorders
- Dialectical Behavioral Therapy (DBT) for personality disorders, chronically suicidal patients, teaches Distress Tolerance Skills
- Motivational Interviewing – for health behavior change including smoking, weight loss, alcohol use, exercise
- Behavioral Activation – great for patients that are “stuck”

SMOKING



From: Cigarette Smoking Among Persons With Schizophrenia or Bipolar Disorder in Routine Clinical Settings, 1999–2011

Psychiatric Services. 2013;64(1):44-50. doi:10.1176/appi.ps.201200143



Same rate but decrease consumption (smoking fewer ppd) in patients with Schizophrenia Cigarette prices leading to this?

Figure Legend:

Quantity of cigarettes consumed (packs per day) by smokers with schizophrenia, by year of study enrollment^{aa}Number of smokers per year: 1999, 10; 2000, 11; 2001, 5; 2002, 20; 2003, 20; 2004, 10; 2005, 28; 2006, 13; 2007, 19; 2008, 30; 2009, 53; 2010, 24; 2011, 23

Smoking and Drug Metabolism

- Increases metabolism at CYP450 A12 so lowers drug level of olanzapine, clozapine
- 7-12 cigs to cause induction
- Need to watch if stop smoking or go to non smoking inpatient treatment setting
- *We give medications that block Dopamine and smoking increases dopamine so patients feel it makes them feel less “dull”. Depressed patients find it helps their mood. Also – remember smoking is an appetite suppressant*

Smoking Cessation – Use your Team

2 mg per day
Watch for
Suicidal
Ideation



21 mg/day
Watch for smoking
while using



Psychosocial Supports
(Case Manager, Peers)



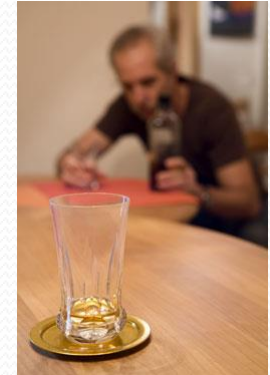
300 mg/day-
Watch for
Activation
10-12 weeks



PORT Guidelines, June 2010

Alcohol Treatment

- Double Trouble, Peer Run Groups, AA
- Naltrexone - 50 – 100 mg per day
 - (watch hepatic functions)
- Vivitrol – injectable naltrexone
- Campral - 333 mg, 2 tid
 - (renal impairment)
- Antabuse - 250 mg per day



Spirit of Motivational Interviewing

“People are generally better persuaded by the reasons that they themselves discovered than by those which have come into the mind of others.”

17th Century French Polymath Blaise Pascal – in
Pensées

Roles for the Psychiatric Providers

Co-Management

- Each provider has their own caseload
- PCP manages all medical problems
- Psychiatrist manages all mental health problems
- Work together to re-enforce treatment plans

Manage with Primary Care Consult

- Psychiatrist works with a care manager
- Manages a caseload of patients for BOTH mental health and basic medical health concerns using protocols from PCP
- PCP available for consultation and stepped care as needed

Comprehensive Management

- Typically dually trained psychiatrist – Psych/FP, Psych/IM, Child Psych/Peds
- Provider manages both medical and mental health problems
- Limited number of providers have this expertise

All psychiatrists are responsible for “not making people sicker”.

Psychiatric Providers' Duties and Responsibilities

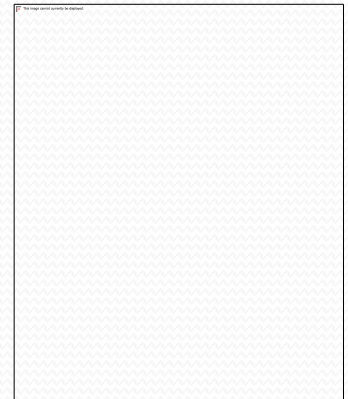
- **Minimize**: Effects of SGAs and other psychotropic medications
- **Screen**: For Illness (APA/ADA Guidelines, etc.), others
- **Counsel**: Lifestyle Modification – smoking, weight loss
- **Treat**: Some Chronic Medical Conditions – “low hanging fruit”?
- **Lead Teams**: trained in both medical and behavioral health worlds

Engage Psychiatric Providers

- Shared patients, shared illnesses – they can counsel, switch meds, minimize side effects, treat
- Patients see them as their “doctor” and may want their approval first
- Complications of psych meds and medical comorbidities
- Staffings for complicated patients
- Go to medical staff meetings – be part of their team
- Educate – help restore their dormant skills in treating chronic medical problems – make them (and you) more well-rounded medical providers

Working with Psychiatric Providers

- Some places have no nurses, no MAs and psych feel stressed about trying to do this all themselves with scales and blood pressure cuffs
- Fickle at times, insecure about medical skills
- Uncomfortable treating other medical problems “out of my scope of practice”, “not safe”. Liability concerns.
- Check in with each other before changing each others meds, agree on changes
- May see this as intrusive meddling instead of much needed support? These are “their” pts
- Trust, humility and teamwork
- ***We’re on the same team so lot of potential for successful partnerships!***



Examples – Working with Psychiatric Providers

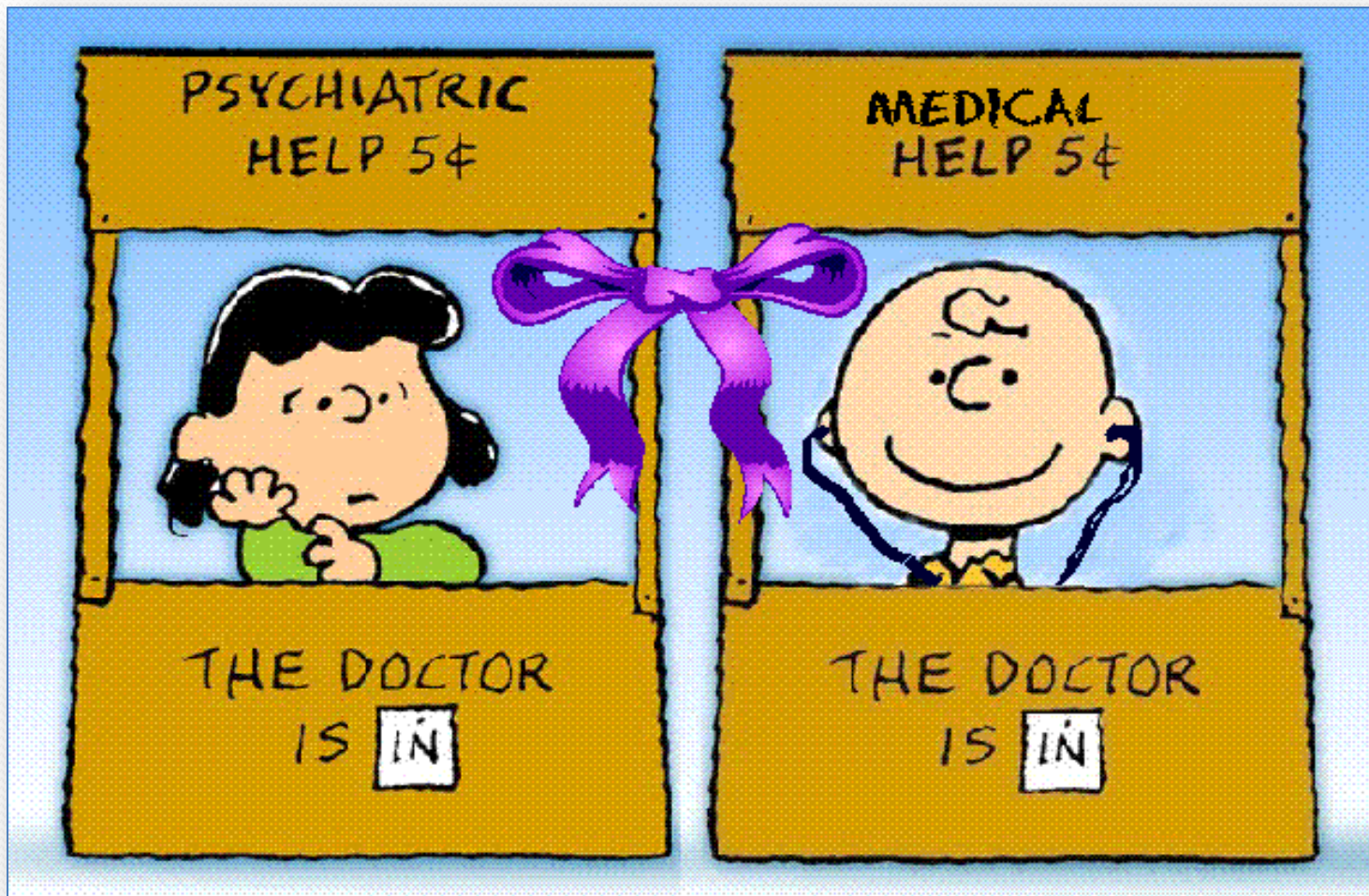
- Psych A is community psychiatrist that has been working for the past 12 years with patients in an urban setting. She feels constrained by the 15 minute med check environment and wishes that she has more time to talk with her patient's and develop a therapeutic alliance more often. She feels that checking vital signs, weighing the patient and talking about lifestyle changes is impossible without more staff and time for patient interaction. Her patients have a number of complex medical problems. She does not have time to call and discuss patients since she does not have a nurse or MA assistant. She has a 16 week back log for new patients.

Examples - continued

- Psych B did a residency in internal medicine and then psychiatry. He has worked for the past 15 yrs only as a psychiatrist and never recertified for internal med. He feels comfortable refilling medications for blood pressure and diabetes in his patients that don't have a PCP however, recently, he is getting a concerned about the new medications and new tests coming out for treatment of HTN and DM. He feels he has no other choice since his patients will only come to see him and no other doctor.

Example - continued

- Psych C: has managed a CTT/ACT team for 5 years. She lost 4 patients last year to heart attack and cancer. She became frustrated by the lack of PCP's in her area that would see her patients or take the time to manage their medical problems. She has been working with two family practice doctors to develop a working relationship. She has exchanged secure email, and cell phone numbers with these providers and they talk about patient care regularly to coordinate medications and test results.



**Partners in Health - Primary Care/County Mental Health Collaboration Toolkit, Integrated Behavioral Health Project (IBHP), October 2009*

Reflections

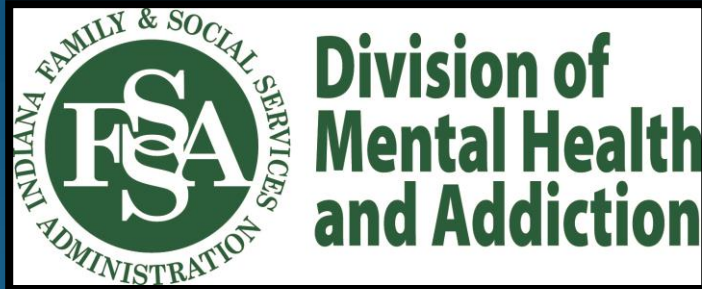
- What do you see as the boundaries of care with your psychiatric colleagues?
- What might be a best approach to discussing care concerns, such as a patient with cardiovascular disease on olanzapine, with psychiatric provider?

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Resources and additional training tools will be available on an elearning system at:

www.indianaintegration.org